

JUL 14 1987

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Interim Report on IARC Rat Chronic
Feeding/Oncogenicity Study on Atrazine Conducted
in Hungary
EPA Registration No. 100-529

Caswell No. 63
Tox Br. Proj. No. 7-0768

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Background

The registrant, Ciba-Geigy, had indicated that IARC was in the process of completing an oncogenicity study of atrazine in rats. This submission is a continuing report on that study.

Results Reported

Preliminary results were reported in a letter from Dr. Borzsonyi of the Hungarian Institute of Hygiene dated May 5, 1987 to Dr. Robert Hess, Ciba-Geigy Inc., Basel.

1. The Fischer 344/LATI (Hungary) strain rat (51 to 56 per sex/group) were test animals.
2. The test material was technical atrazine 98.9% pure Batch No. 004124 provided by Ciba-Geigy (Basel).

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3. Treatment was dietary at 1000 and 500 ppm for 8 weeks then lowered (because of toxicity) to 750 and 375 ppm respectively. The animals were treated for life.
4. Results - Dose-related (nonstatistically significant) decreases in body weights of both sexes.
5. Controls - Males showed decreased survival rates.
6. Treated Males - A non-statistically significant increase (dose-related) in combined leukemia/lymphoma was noted.

Controls: 22/47

Low: 27/47

High: 32/48

Benign mammary tumors in males.

Controls: 1/48

Low: 1/51

High: 9/53 (includes 1 carcinoma)

(The difference was significant with Peto's incidental tumor test.)

7. Treated Females: Dose-related and statistically significant (Cochran-Armitage linear trend test) increase in leukemia/lymphoma was noted.

Controls: 12/44

Low: 16/52

High: 22/51

Uterine adenocarcinomas were increased and statistically significant (Cochran-Armitage linear trend test).

Controls: 7/45

Low: 10/52

High: 14/45

However, benign uterine polyps indicated a negative trend.

Controls: 9/45

Low: 9/52

High: 3/45

3. No chronic toxicity signs were noted.

9. Dr. Borzsonyi indicated that to his knowledge this was the first long-term bioassay with this strain and no real comparison with historical controls could be made. His overall assessment was as follows.

ATRAZINE proved to be carcinogenic in the above described experimental conditions. We consider it as a weak carcinogen since:

- mammary gland tumors observed in the high dose group were benign fibroadenomas or adenomas;
- leukaemias/lumphomas are common in both male and female Fischer rats, therefore the statistically significant increase in femals should be cautiously evaluated;
- malignant uterine tumors might represent late developmental stage originated from benign polyps. Malignant uterine tumors appear to be fairly rare in this strain; however they could be regarded as a late stage of malignisation of benign polyps.

Conclusions

Toxicology Branch (TB) recognizes that the entire study report is required for evaluation and that this report is only supplemental information.

TB also notes that the authors consider the study to support atrazine as a weak carcinogen in the experiment.